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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Serial No. 10/677,734

Customer No. 23379

Applicant: Gardner et al.

Confirmation No. 4912

Filed: Oct 01, 2003

Group Art Unit: 1645

Docket No. UTSD:1510-1

Examiner: Swope, Sheridan

Title: *Foreign PAS Ligands Regulate PAS
Domain Function*

CERTIFICATE OF TRANSMISSION
I hereby certify that this corr is being transmitted by facsimile to
the Comm for Patents 571-273-8300 on December 20, 2005.
Signed Richard Afon Osman

RESPONSE

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Commissioner:

Thank you for the Action dated Dec 13, 2005; pursuant to the attached Request for
Continued Examination, please enter these amendments:

Please amend the paragraph at p.4, lines 13-20 as follows:

In one aspect of the invention, we show that foreign ligands can be introduced into the hydrophobic core regions of PAS domains even (a) where the PAS domain does not require a core-bound ligand for formation or function; (b) the PAS domain is fully folded in its native state; c) where there is no NMR-apparent a priori formed core cavity to accommodate such a ligand; and/or (d) wherein the PAS domain is unassociated with any predetermined ligand-dependent heterologous chaperone protein. In contrast, AHR PAS-B binds both HSP90, a common chaperone of unfolded proteins, and ligand, and the AHR PAS-B domain is unfolded without ligand (e.g. Kikuchi, et al., 2003, J Biochem 134, 83-90).

Please amend the paragraph bridging p.15 and p.16 as follows:

The first PAS domain protein for which a ligand binding site discovery was made using this library is the PAS A domain of PAS Kinase. The kinase domain of this protein, involved in regulation of sugar metabolism and translation (~~Rutter et al., 2002~~), is partially inhibited by direct interaction with its N-terminal PAS domain. We have recently reported that a series of diphenylmethanes, found during a NMR screen (Amezcuca et al., 2002), selectively bind at the same site where heme and flavin mononucleotide (FMN) are localized in the crystal structures of FixL (Gong et al., 1998; Miyatake et al., 2000) and Phy3 (Crosson & Moffat, 2001) respectively. The latter two proteins are also PAS-containing kinases regulated by their PAS domains. This discovery, together with our mutational and biochemical studies, ~~informs~~ elucidates the mode of kinase regulation by the PAS domain.

Immediately after p.24, line 30, please delete the paragraph as follows:

~~Rutter J, Probst BL, McKnight SL (2002) Coordinate regulation of sugar flux and translation by PAS kinase. Cell. 111(1):17-28.~~